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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/885,679	PERA, MARTIN FREDERICK	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed June 20, 2001 claims benefit to foreign applications PR1327, filed November 8, 2000, and PQ8242, filed June 20, 2000, both in Australia.

Applicants' amendment filed September 10, 2004 has been received and entered. Claims 1-49 have been canceled. Claims 50-67 have been added. Claims 50-67 are pending.

Election/Restriction

Applicant's election with traverse of group I, and the election of species of noggin in Paper No. 11 was acknowledged. The requirement was deemed proper and made FINAL. No new grounds of traversal have been provided. The newly added claims broadly encompass any species of antagonist, however for the purpose of examination will be examined to the extent they encompass the elected species of noggin.

Claims 50-67 are pending and currently under examination as they are drawn to methods of culturing ES cells with the BMP antagonist noggin.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications PR1327 and PQ8242 filed in Australia on November 8, 2000 and June 20, 2000, respectively. Review of the file has indicated that a certified copy of the Australian applications as required by 35 U.S.C. 119(b) was been filed December 8, 2003.

Specification

The abstract of the disclosure stands objected to because it is not present as a single paragraph. Correction is required. See MPEP § 608.01(b).

Applicants have not amended the abstract of the specification therefore, the objection stands for the reasons of record. Again, Applicant is reminded of the proper language and format for an abstract of the disclosure. The abstract should be in narrative form limited to a single paragraph on a separate sheet within the range of 50 -150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Newly added claims 50-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-15 and 20 of copending Application No. 09/670,198. Initially, it is noted that in 09/670,198 Applicants have elected methods of culturing pluripotential cells and compositions for practicing said methods (see restriction requirement, paper number 6, and election paper, number 8). Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the methods are drawn to methods of culturing comprising the same steps and using noggin as an antagonist/inhibitor of the BMP pathway. Each set of claims set forth obtaining a source of pluripotential cells and the dependent claims of 09/670,198 specifically recite that ES cells are a contemplated source. Further, each set of claims set forth inhibiting the BMP pathway, and in each application dependent claims specifically set forth that the agent used is noggin.

It is noted that Applicants have not addressed the basis of the rejection in their instant amendment. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50-56, 59-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of culturing human embryonic stem (ES) cells comprising: (1) obtaining a source of human ES cells; and (2) providing culturing conditions of said human ES cells in the presence of noggin for 5 days wherein said conditions result in an undifferentiated cell which does not express ES stem cell markers, does not reasonably provide enablement for methods for producing progenitor cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice and make the invention commensurate in scope with these claims.

The amendment to the claims to encompass the use of human ES cells is noted, and the rejection as it encompasses this embodiment is withdrawn. The basis of the rejection focuses on one remaining issue, namely what type of cell is produced by the methods disclosed in the instant specification. As stated in the previous office action, the nature of the resulting cells after practicing the specific method steps of culturing ES cells with an antagonist of a BMP pathway, in particular treating the cells with the elected species of noggin. The specification provides evidence that human ES cells treated with noggin for 5 days results in a cell lacking the original stem cell markers and guidance to use this resulting noggin treated cell to produce neuronal progenitor cells and potentially other cell types. The art of record indicates that noggin may be important in differentiation into neuronal cell types, however it exact role and specific affects are still not adequately defined. Given the guidance in the specification and the evidence of record,

only methods of culturing human embryonic stem (ES) cells comprising: (1) obtaining a source of human ES cells; and (2) providing culturing conditions of said human ES cells in the presence of noggin for 5 days wherein said conditions result in an undifferentiated cell which does not express ES stem cell markers are enabled. With respect to the using the methods as instantly claimed for producing "a progenitor cell", as noted above, the specification acknowledges that treating human ES cells with noggin results in a cell has not been fully characterized. Lacking neuronal cell markers the specification asserts it is not a neuronal progenitor cell. The specification provides evidence that the noggin treated human ES cell are capable of differentiating into neuronal and glial cells, not broadly into progenitor cells as required by the claims. Furthermore it should be noted that the specification teaches that the resulting noggin treated human ES cell can be used for a "facile route to the isolation of neuronal progenitors" (page 29, lines 13-14). In light of the lack of neuronal markers and the lack of stem cell markers, the noggin treated cell appears to be an intermediate cell type. The ability of the resulting cell to differentiate into neuronal cell types is consistent with the activity previously known and described for noggin and BMP-2. For example, as stated previously both Gratsch *et al.* and Carpenter *et al.* teach that noggin is a neurotrophic factor and in the characterization of recombinant human noggin, Carpenter *et al.* demonstrate that noggin alone is capable of driving neuronal induction in developing embryos (column 25, lines 15-50; and results summarized by figures 4 and 6). Thus, at the time of filing, noggin was known in the art to be a neurogenic factor affecting BMP-2 and important in neuronal differentiation. Examiner does not contend that the one could not simply culture cells with noggin, nor that prolonged culturing with a neurotrophic factor would result in the formation of cells of neuronal cell lineages as this is

supported by the art of record. Rather, what is supported by the present specification is that the culturing of human ES cells for 5 days provides an intermediate cell type before complete differentiation into a neuronal cell. Though generally this is not unexpected because the culturing of an undifferentiated cell into a differentiated cell must proceed through the process of differentiation providing intermediate cell types or at least phenotypes not representative of either a completely undifferentiated or differentiated cell type.

Again it is noted that the courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. 27 USPQ2d 1662 *Ex parte Maizel.* In this case, practicing the claimed methods is facile, however given the lack of characterization of the resulting noggin treated cell as acknowledged by the specification there is not objective evidence that the resulting noggin treated cell is a progenitor capable of giving rise to any somatic lineage. Given the complexity of the BMP pathway recognized in the art and the affect of noggin on ES cells from other species, the only defining character of the resulting cell considered adequately defined would be the cell lacking the original ES cell markers. As taught by the specification this noggin treated cell type can be used to produce neuronal progenitor cells.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 57, 58, 66 and 67 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (US Patent 5,843,780).

Applicants summarize the basis of the rejection, note that the previous claims have been canceled, and argue that the instantly claimed cells can be distinguished from those taught by Thomson because a 'progenitor cell lacks at least one marker' of an undifferentiated cell (page 8). See pages 7-9. Applicants' arguments have been fully considered, but not found persuasive.

First, it is noted that the claims broadly encompass any progenitor cell made by any method. As noted previously a progenitor cell is not specifically defined in the specification, however within the context of the methods the term is described as a "cell which is capable of differentiation into any somatic lineage" (page 14, lines 24-26). Upon review of the specification Examiner can not identify support for Applicants argument that a progenitor cell is defined as lacking at least one marker of an undifferentiated stem cell. Furthermore, there is no guidance nor support in the specification for which cell marker would define this change from stem cell to progenitor cell. The claim is being given its broadest most reasonable interpretation

in light of the teachings of the specification and the art of record. The term "progenitor cell" as recognized in the art is a general term which is consistent with that set forth in the specification as cited above, and for the purposes of art rejections is being interpreted by the functional ability of the cell to give rise to any somatic cell lineage. In this case, because embryonic stem cells are capable of giving rise to any somatic cell lineage, an ES cell is being interpreted to be a type of progenitor cell.

As summarized previously, Thomson teach primate embryonic stem cells. The stem cells are pluripotent capable of giving rise to the various somatic cell lineages which is demonstrated by injecting the cells into a SCID mouse and analyzing the resulting cell types (column 11, lines 12-58). Thus, the anticipate the ES/progenitor cells encompassed by claims 1, 2 and 15. With respect to the specific antibody markers set forth in claim 15, it is noted that Thomson does not specifically analyze for the presence or absence of these cell surface markers, however as recognized in the art and indicated in the present specification they represent markers on ES cell cultures which are allowed to spontaneously differentiate and are present at early time points of 7-10 days in culture (page 13, lines 20-30). Because the primate ES cells described by Thomson are highly pluripotent and not subject to differentiating conditions in culture, they would not have any of these cell surface markers. Moreover, with respect to the ES cells as claimed as a product by process (claims 13, 14, 29), where, as here, the claimed and prior art products are identical or substantially identical, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is

evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown,* 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). With respect to the methods wherein the ES cells are cultured in the presence of noggin or where noggin is used to produce a progenitor cell, any particular affect of these methods on the ES or resulting progenitor cell to differentiate from that known in the art is not set forth. Therefore in this case, the undifferentiated ES cells and progenitor cells being claimed are being interpreted to be cells defined by their functional properties which are cells capable of giving rise to any cell type of any lineage. As noted above, Thomson teach that the primate embyronic stem cells are pluripotent and capable of giving rise to the various somatic cell lineages which was demonstrated by injecting the ES cells into a SCID mouse and analyzing the resulting cell types (column 11, lines 12-58). Since the ES cells described by Thomson have the phenotypic characteristics of ES/progenitor cells recognized in the art as defined and supported by the instant specification, the primate ES cells described by Thomson anticipate the instantly claimed ES/progenitor cells which were cultured in the presence of noggin.

Importantly, the present specification acknowledges that even the specific cell type produced in the working example has not fully characterized. Given the limited disclosure of the cells produced by the claimed methods and the breadth of the types of cells encompassed by the terms as recognized in the art, it is maintained that the cells taught by Thomson anticipate the instantly claimed cells.

Claims 57, 58, 66 and 67 are rejected under 35 U.S.C. 102(e) as being anticipated by Carpenter *et al.* (Pub. No. US2002/0019046 A1).

Applicants summarize the teachings of Carpenter *et al.* (page 9) and argue that the disclosure for the use of noggin in the priority documents first appears in US2002/0019046, not any of the provisional applications thus does not qualify as a 102(e) type reference. See pages 9-10. Applicants' arguments have been fully considered, but not found persuasive.

The priority information is noted, however the teachings of Carpenter *et al.* relied upon for the instant rejection is the teaching of human embryonic stem cells, not the methodology. As stated above the term "progenitor cell" for the purposes of art rejections is being interpreted by the functional ability of the cell to give rise to any somatic cell lineage. Further, as reasoned above, because embryonic stem cells are capable of giving rise to any somatic cell lineage, an ES cell is being interpreted to be a type of progenitor cell. Carpenter *et al.* teach primate pluripotent stem cells, and specifically teach that embryonic stem cells as taught by Thomson (page 4, paragraphs 45-48, in particular paragraph 46). Thus, to the extent that the instantly claimed products encompass embryonic stem cells, the pluripotential embryonic stem cells taught by Carpenter *et al.* anticipate claims 57, 58, 66 and 67.

As noted above in the rejection over Thomson, the present specification acknowledges that even the specific cell type produced in the working example has not fully characterized. Given the limited disclosure of the cells produced by the claimed methods and the breadth of the types of cells encompassed by the terms as recognized in the art, it is maintained that the cells taught by Carpenter *et al.* anticipate the instantly claimed cells.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach